



Global Leader in Allogeneic Cellular Medicines for Inflammatory Diseases

Corporate Presentation
BIOTECH SHOWCASE 2023

January 2023

ASX: MSB; Nasdaq: MESO



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Our Mission

Mesoblast is committed to bringing to market innovative cellular medicines to treat serious and life-threatening illnesses



Investment Highlights

First FDA Approval Expected in 2023

Potential 2023 Launch for Remestemcel-L/SR-aGVHD

Remestemcel-L BLA to be resubmitted for children with steroid-refractory acute graft versus host disease (SR-aGVHD), with potential US approval in mid-CY2023

Innovative Late-Stage Pipeline

Rexlemestrocel-L progressing towards initiation of a second pivotal Phase 3 study commencing H1 CY2023 for discogenic chronic low back pain (CLBP), followed by chronic heart failure with reduced ejection fraction (HFrEF)

Novel Allogeneic Cell Therapy Platform

Developing an off-the-shelf, allogeneic cell therapy platform based on mesenchymal stromal cell technology to enable treatment without the need for donor matching or immunosuppression

Cash Resources to Support Operations thru 2023+

Cash-on-hand of US\$85.5 million plus up to an additional US\$40 million from existing financing facilities, subject to certain milestones, with potential upside from partnering income

Remestemcel-L / SR-aGVHD

Biologics License Application (BLA) Resubmission Milestones

Updated FDA IND File in Oct-22

Submitted substantial new information on clinical and potency assay items identified in the CRL received from FDA in 2020 to Investigational New Drug (IND) file for remestemcel-L in the treatment of children with SR-aGVHD

New Long-term Survival Data from Phase 3 trial

In Nov-22 released long-term survival results from pivotal trial showing durable survival through 4 years of follow-up. These new long-term survival data are a key component of the BLA resubmission

Potency Assay Work Completed

Optimization and validation work completed on the potency assay that was in place at the time of the Phase 3 trial and which demonstrates a relationship between the product's activity in-vitro and its effects on survival, addressing a key component of CRL

Currently in Publishing, ahead of Resubmission

Final drafting of the BLA is complete and the document is with the publisher for filing

Late-Stage Clinical Pipeline

Based on the Proprietary Allogeneic Mesenchymal Stromal Cell Platform

Product	Indication	Phase 2	Phase 3	Regulatory Filing	Approved	Status/Next Steps	
Remestemcel-L	SR-aGVHD						<ul style="list-style-type: none"> • BLA to be resubmitted • Planning for a mid-CY2023 launch
Rexlemestrocel-L	CLBP						<ul style="list-style-type: none"> • Finalizing Phase 3 protocol • Planning to start a pivotal Phase 3 program in H1 CY2023
Rexlemestrocel-L	HFrEF						<ul style="list-style-type: none"> • FDA meeting planned for H1 CY2023
Remestemcel-L	ARDS and other applications						<ul style="list-style-type: none"> • Clinical collaborations, investigator studies

Mesoblast's Proprietary Stem Cell Technology

Based on mesenchymal lineage adult stem cells (MLCs/SCs)



Mesenchymal Lineage

MLCs are **derived** from healthy bone marrow, **present** around blood vessels and **responsive** to signals associated with tissue damage / inflammation



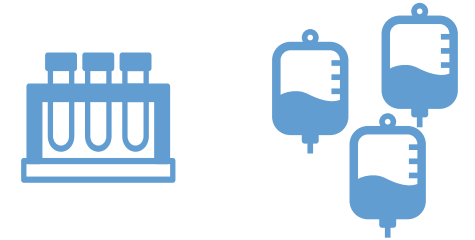
Defined Stem Cells

Biologically-defined, optimized for results:
Remestemcel-L: based on mesenchymal stromal cells (MSCs)
Rexlemestemcel-L: based on mesenchymal precursor cells (MPCs)



Allogenic Properties

Expanded **without differentiation**
No expression of cell surface co-stimulatory molecules



Scalable Production

Scalable “off-the-shelf” cellular platforms
Validated potency assay to ensure batch-to-batch consistency and reproducibility

Remestemcel-L

Steroid-Refractory Acute
Graft Versus Host Disease (SR-
aGVHD)

*BLA to be resubmitted. Tracking to a
potential mid-CY2023 approval*



Remestemcel-L: Steroid-Refractory Acute Graft Versus Host Disease (SR-aGVHD)

SR-aGVHD is associated with mortality rates as high as 90%

Treatment Options

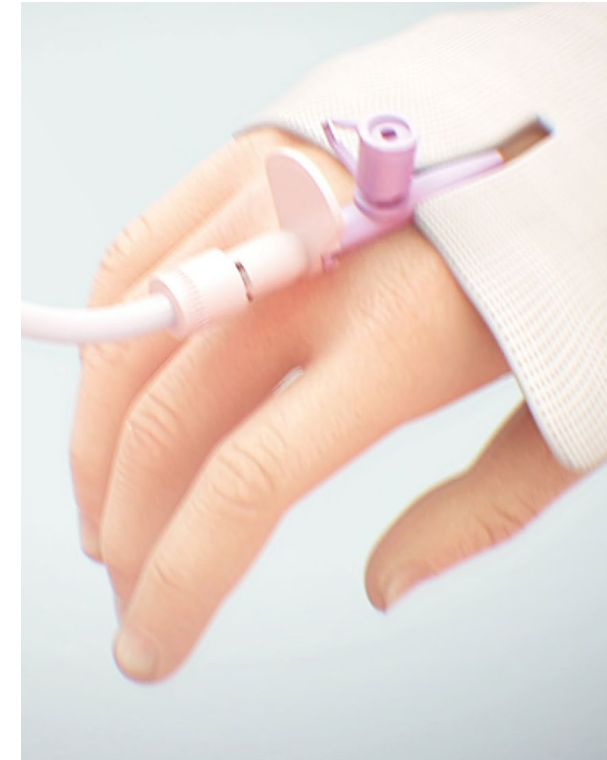
- Corticosteroids are first-line therapy for aGVHD
- There is only one approved treatment for disease refractory to steroids and no approved treatment in the US for children under 12 years old
- In Japan, Mesoblast's licensee has received the only product approval for SR-aGVHD in both children and adults

Burden of Illness

- Acute GVHD is a life-threatening complication that occurs in ~50% of patients receiving allogeneic bone marrow transplants (BMTs)¹
- Acute GVHD primarily affects skin, GI tract, and liver
- Steroid-refractory aGVHD is associated with mortality rates as high as 90%^{1,5} and significant extended hospital stay costs²

Market Opportunity

- More than 30,000 allogeneic BMTs performed globally (>20K US/EU) annually, ~20% pediatric^{3,4}
- Approx. 1,500 allogeneic BMTs in children and adolescents in US⁴



1. Westin, J., Saliba, RM., Lima, M. (2011) Steroid-refractory acute GVHD: predictors and outcomes. *Advances in Hematology*. 2. Anthem-HealthCore/Mesoblast claims analysis (2016). Data on file 3. Niederwieser D, Baldomero H, Szer J. (2016) Hematopoietic stem cell transplantation activity worldwide in 2012 and a SWOT analysis of the Worldwide Network for Blood and Marrow Transplantation Group including the global survey. 4. HRSA Transplant Activity Report, CIBMTR, 2019 5. Axt L, Naumann A, Toennies J (2019) Retrospective single center analysis of outcome, risk factors and therapy in steroid refractory graft-versus-host disease after allogeneic hematopoietic cell transplantation. *Bone Marrow Transplantation*.

Remestemcel-L for SR-aGVHD

Improved Early Survival in Children Across Three Studies

Day 100 Survival			
Remestemcel-L Protocol	Remestemcel-L	Matched Controls	Matched Control Protocol
First Line Therapy after Steroids Treatment Setting			
Pediatric Subset of Protocol 280: randomized controlled P3, n=27 w/SR-aGVHD	79%	54%	Study Control Arm (n=13)
Study 001, open-label P3, n=54 ¹ with 89% Grade C/D disease	74%	57%	MAGIC ² cohort, n=30 ³ propensity-controlled subset
Salvage Therapy Treatment Setting			
Expanded Access Protocol (EAP275), n=241	66%	na	
EAP275, n=51 Grade D subset	51%	31%	CIBMTR dbase, n=327 ⁴ propensity controlled subset

1. GVHD001 had 55 randomized patients, however one patient dropped out before receiving any dose of remestemcel-L; 2. Mount Sinai Acute GVHD International Consortium (MAGIC) - a group of ten BMT centers throughout the US and Europe whose purpose is to conduct ground-breaking clinical trials in GVHD, including developing informative biorepositories that assist in developing treatments that can guide GVHD therapy; 3. Two subjects in the MAGIC cohort had follow-up <100 days; these subjects are excluded from the respective survival analyses; 4. Data on file

Extended Survival Data in Children with SR-aGVHD

Remestemcel-L Treatment Resulted in Consistent and Durable Responses Over 4 Years

Survival Comparison

(Remestemcel-L data from the Center for International Blood and Marrow Transplant Research (CIBMTR) dbase)

Study	GVHD001	MacMillan et al ¹	Rashidi et al ²	Zeiser et al ³	REACH2 ³	REACH1 ⁴
Treatment	Remestemcel-L	BAT ⁵	BAT ⁵	BAT ⁵	Ruxolitinib	Ruxolitinib
N=	51	128	203	155	154	71
Subjects	Children	Children	Adults	Adults	Adults	Adults
aGVHD Grade	88% Grade C/D	22% Grade 3/4	54% Grade 3/4	63% Grade 3/4	63% Grade 3/4	68% Grade 3/4
Year 1 Survival	63%	40%	--	44%	49%	43%
Year 2 Survival	51%	35%	25%	36%	38%	--
Year 3 Survival	49%					
Year 4 Survival	49%					

1. MacMillan ML et al. Pediatric acute GVHD: clinical phenotype and response to upfront steroids. Bone Marrow Transplant 2020; 55(1): 165-171

2. Rashidi A et al. Outcomes and predictors of response in steroid-refractory acute graft-versus-host disease: single-center results from a cohort of 203 patients. Biol Blood Bone Marrow Transplant 2019; 25(11):2297-2302.

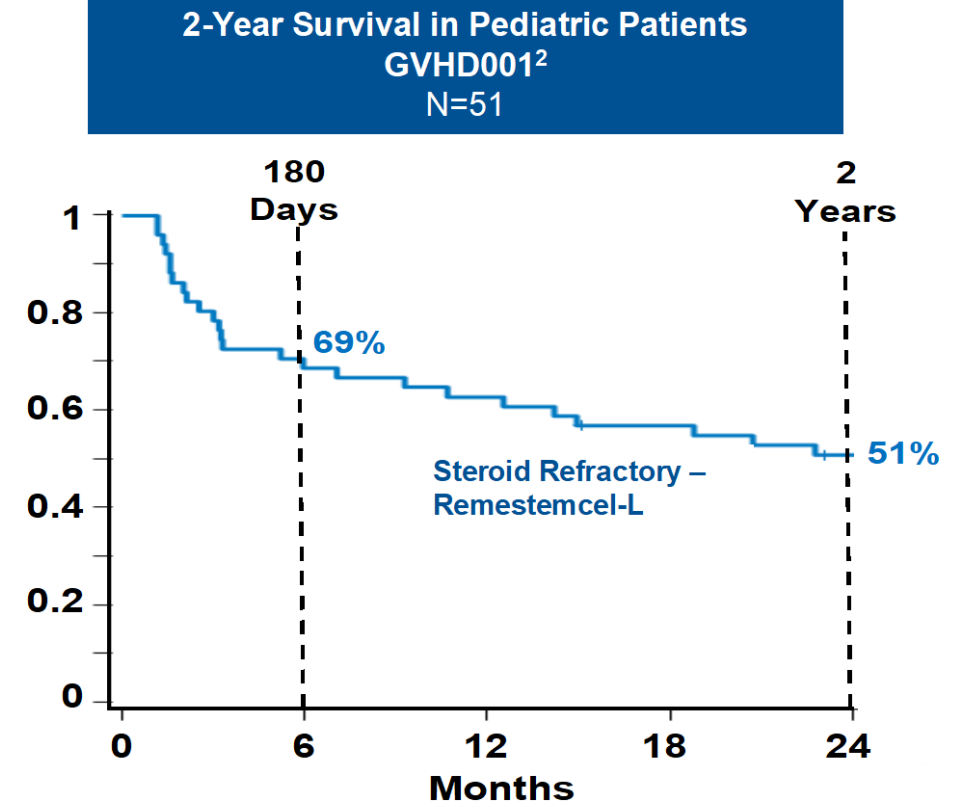
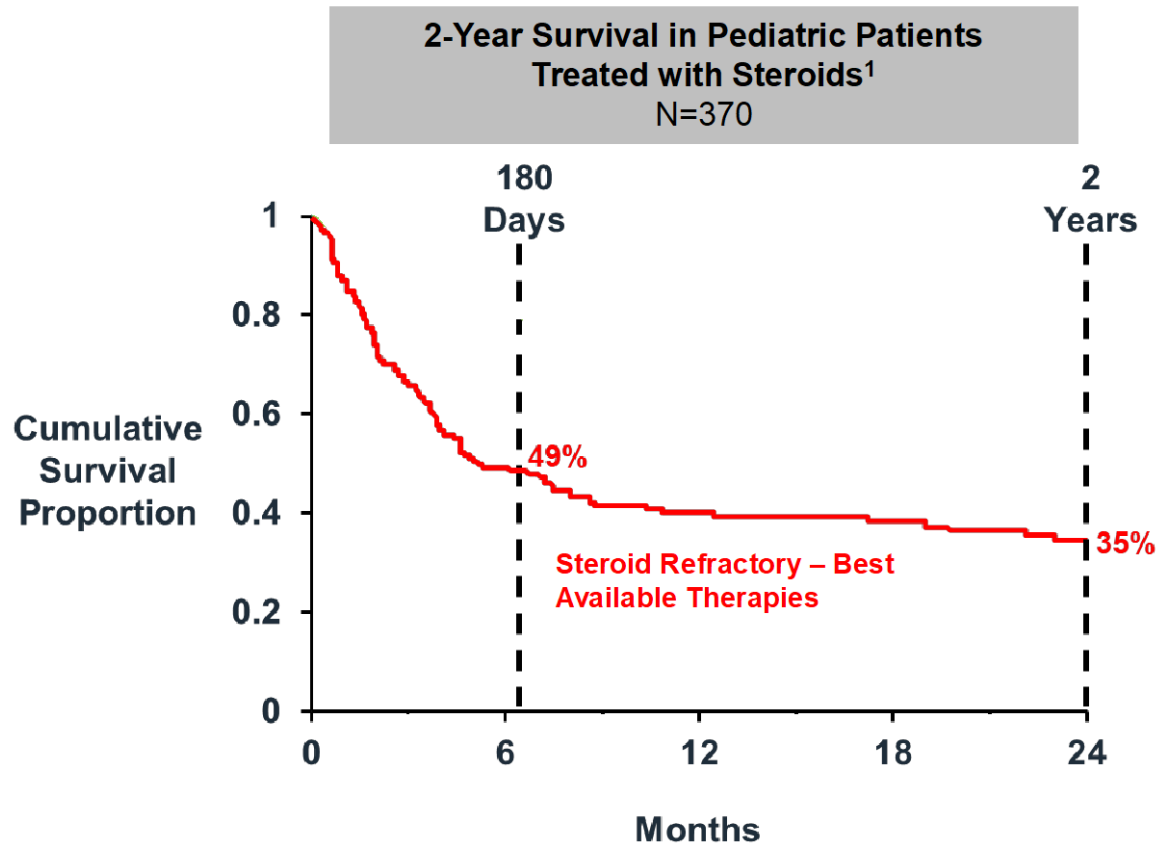
3. Zeiser R et al. Ruxolitinib for Glucocorticoid-Refractory Acute Graft-versus-Host Disease. N Engl J Med 2020;382:1800-10.

4. Jagasia M et al. Ruxolitinib for the treatment of steroid-refractory acute GVHD (REACH1): a multicenter, open-label phase 2 trial. Blood. 2020 May 14; 135(20): 1739–1749

5. BAT = Best Available Treatment

Survival Outlook in Pediatric Patients with SR-aGVHD

Remestemcel has the Potential to Improve Long-Term Survival (>2 Years)

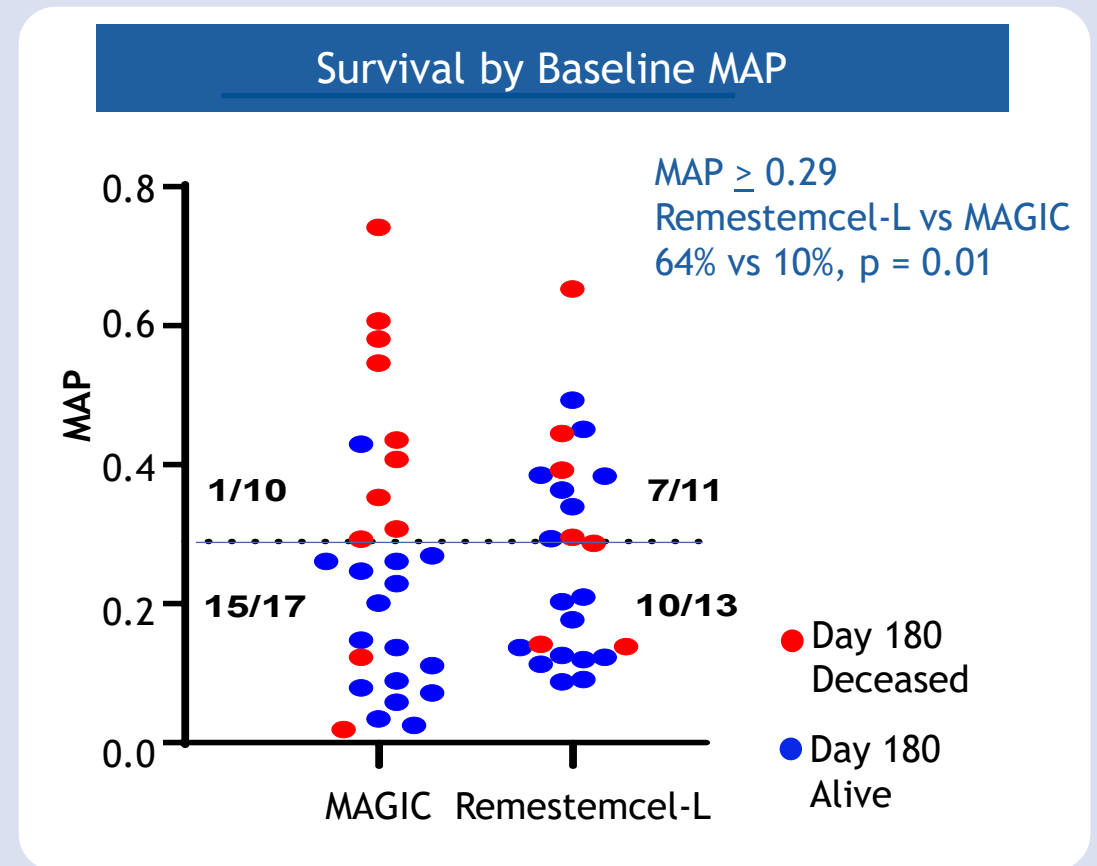
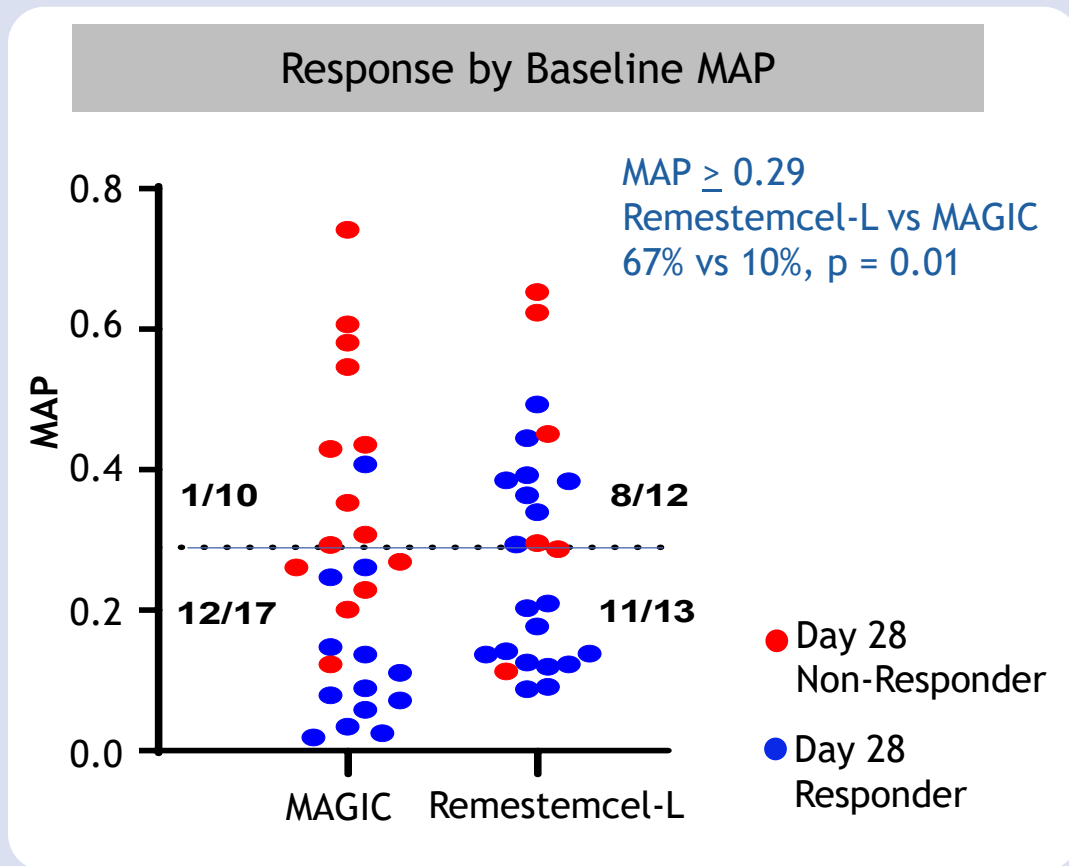


1. Adapted and redrawn from Figure 2 of MacMillan, M.L. et al. Pediatric acute GVHD: clinical phenotype and response to upfront steroids. Bone Marrow Transplant 55, 165–171 (2020);

2. CIBMTR – Center for International Blood & Bone Marrow Transplantation Research. Clinical Outcomes of Pediatric Patients Treated with Remestemcel-L for Steroid-Refractory Acute Graft Versus-Host Disease on a Phase 3, Single-Arm, Prospective Study (Nov 2022)

Remestemcel-L for SR-aGVHD

Significantly Greater Day 28 Overall Responses and Day 180 Survival in Highest-Risk Patients (Baseline MAP ≥ 0.29)



Remestemcel-L / SR-aGVHD

Putting the Pieces in Place for a U.S. Approval



Expanded data

Survival outcomes have not improved over two decades despite BAT

New 4-year survival data from CIBMTR in 51 patients from P3 trial will be a cornerstone of the BLA resubmission



Potency Assay

Optimized, validated a potency assay from the Phase 3 trial demonstrating the relationship between in-vitro activity and survival outcomes is another essential element of the resubmission



Manufacturing readiness

In preparation for the expected FDA review, a mock pre-approval of the GMP manufacturing facility and process inspection was conducted by external auditors



Est. mid-CY2023 Approval

BLA to be resubmitted
Fast Track Designation and BLA Priority Review from the FDA could yield a mid-CY2023 launch

Rexlemestrocel-L

Chronic Low Back Pain
associated with Degenerative
Disc Disease (CLBP)

*Commence Pivotal Phase 3 Study in
CY2023 with Reduction in Pain
Primary Endpoint*



Chronic Low Back Pain Due to Degenerative Disc Disease (CLBP) Impacts 7M+ Rexlemestrocel-L represents a potential new paradigm for the treatment of CLBP

Burden of Illness

- Back pain causes more disability than any other condition¹
- Inflicts substantial direct and indirect costs on the healthcare system,¹ including excessive use of opioids in this patient population

Treatment Options

- Minimal treatment options for patients with chronic low back pain (CLBP) who fail conservative therapy include opioids and surgery
- 50% of opioid prescriptions are for CLBP²
- Durable improvement in pain has potential to reduce opioid use and prevent surgical intervention

Market Opportunity

- Over 7m patients are estimated to suffer from CLBP due to degenerative disc disease (DDD) in each of the U.S. and E.U.³⁻⁴



1. Williams, J., NG, Nawi, Pelzter, K. (2015) Risk factors and disability associated with low back pain in older adults in low-and middle-income countries. Results from the WHO Study on global ageing and adult health (SAGE). PloS One. 2015; 10(6): e0127880., 2. Decision Resources: Chronic Pain December 2015., 3. LEK & NCI opinion leader interviews, and secondary analysis., 4. Navigant: Commercial Assessment for a Proprietary Cell-Based Therapy for DDD in the U.S. and the EU3 - August 2014.

Patients with CLBP Refractory to Standard Treatment Have Minimal Options

Rexlemestrocel-L has Potential to be 1L Treatment for Patients with Moderate to Severe CLBP, Refractory to Conservative Treatment

Rexlemestrocel-L targeting moderate-to-severe CLBP

Conservative Treatments

- NSAIDs
- Physical therapy
- Chiropractic treatments
- Acupuncture
- Anticonvulsants (e.g., gabapentin)

Opioid Analgesics

- Weak opioid analgesics (e.g., tramadol)
- Strong opioid analgesics (e.g., oxycodone)

Interventional Therapies

- Epidural steroid injections (off-label)
- Radio frequency ablation
- Spinal cord stimulation
- Intrathecal pumps

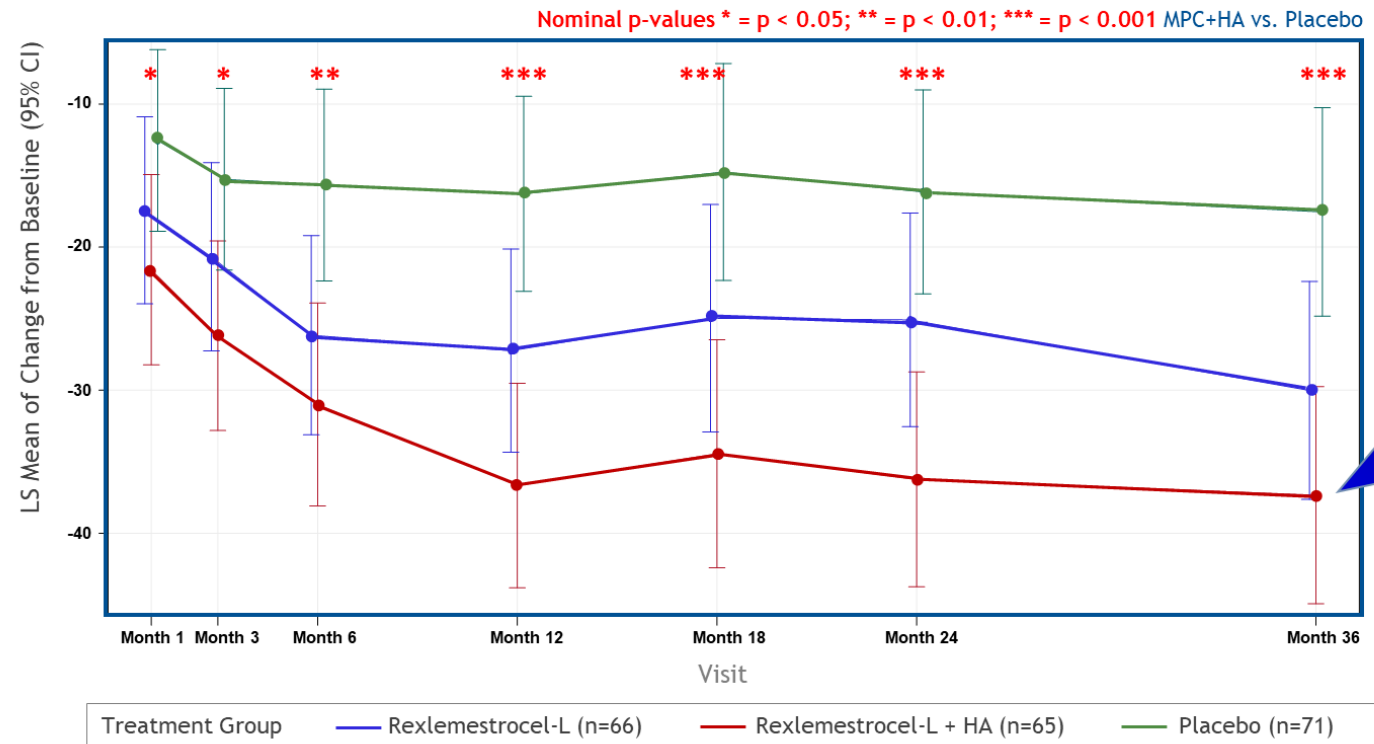
Conservative Treatments

- Spinal fusion
- Disc replacement

Phase 3 Trial Outcomes based on a Single Injection of Rexlemestrocel-L + HA Results in More than Three Years of Pain Reduction

Greatest pain reduction was observed in the pre-specified population of subjects with CLBP duration shorter than the baseline study median of 68 months (n=202) with significantly greater reduction (nominal p-value < 0.05) at all time points analyzed over 36 months compared with saline controls

LS Mean VAS Change in Low Back Pain from Baseline - Duration CLBP < 68 Month Median Baseline Duration (n=202)

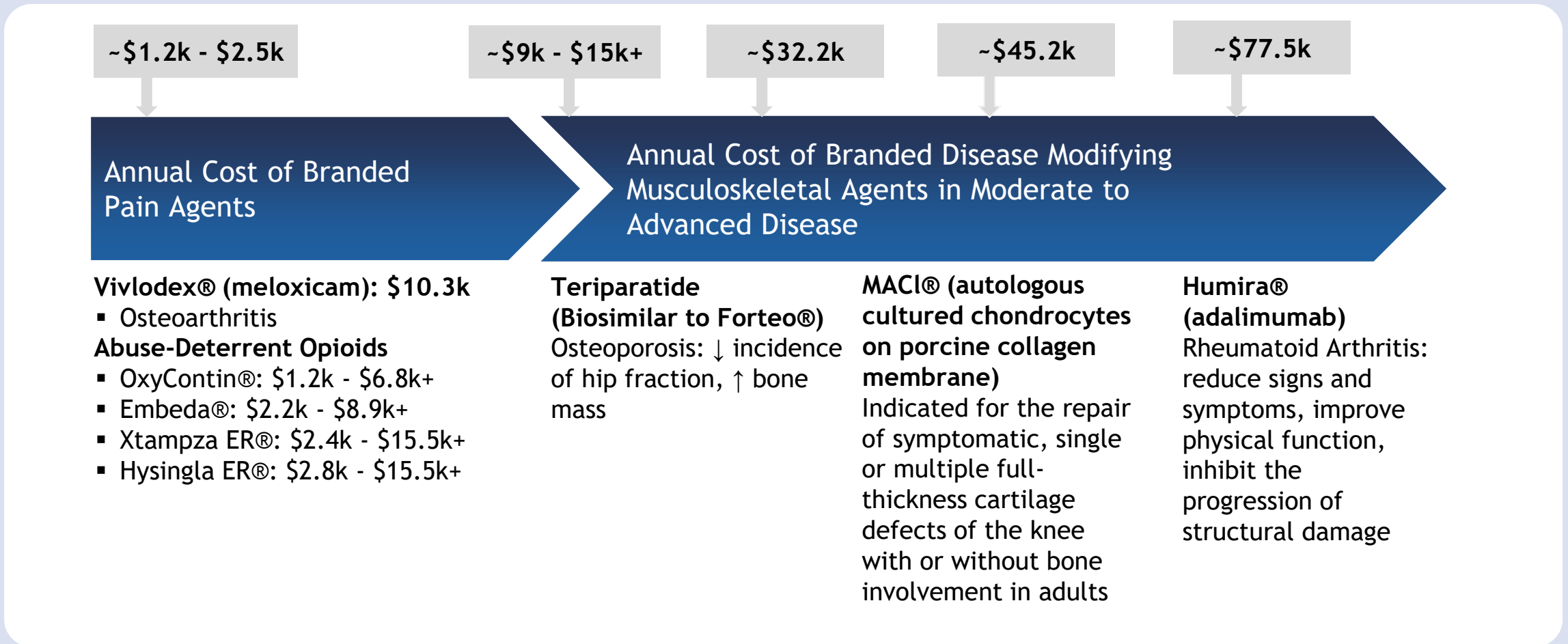


Duration < Median
Rexlemestrocel-L +HA Demonstrated significant reductions in pain over 36-months

VAS=Visual Analog Score; HA=Hyaluronic Acid

Pricing Landscape for Pain Management to Disease Modifying Therapies (DMTs)

Reference Pricing Analysis Suggests Higher US Price Points for DMTs



Rexlemestrocel-L/DCLBP

Preparing to Initiate the Pivotal Phase 3 Program



Regulatory Alignment

Gained alignment with the FDA on the appropriate pivotal Phase 3 study in patients with CLBP which seeks to replicate the significant reduction in pain seen at 12 and 24 months in our first Phase 3 trial



Phase 3 Protocol

FDA has agreed with Mesoblast plans for mean **pain reduction at 12 months as a primary endpoint** of the next pivotal trial

Mean functional improvement and reduction in opioid use as secondary endpoints



In Prep for US/EU Submissions

The planned Phase 3 Program will include 80% of subjects in the US and 20% from the EU, to support regulatory submissions to FDA and EMA



Commence Pivotal P3 H1 CY2023

Awaiting clearance from the FDA to commence the pivotal trial CY2023

Rexlemestrocel-L

Chronic Heart Failure Reduced
Ejection Fraction (HFrEF)

*Tracking to a potential H1 CY2023
FDA meeting to map out pivotal trial
plans and regulatory pathway*



Chronic Heart Failure (CHF): Rising Incidence and High Mortality

New therapies reduce recurrent hospitalization but do not materially improve mortality or major ischemic event rates

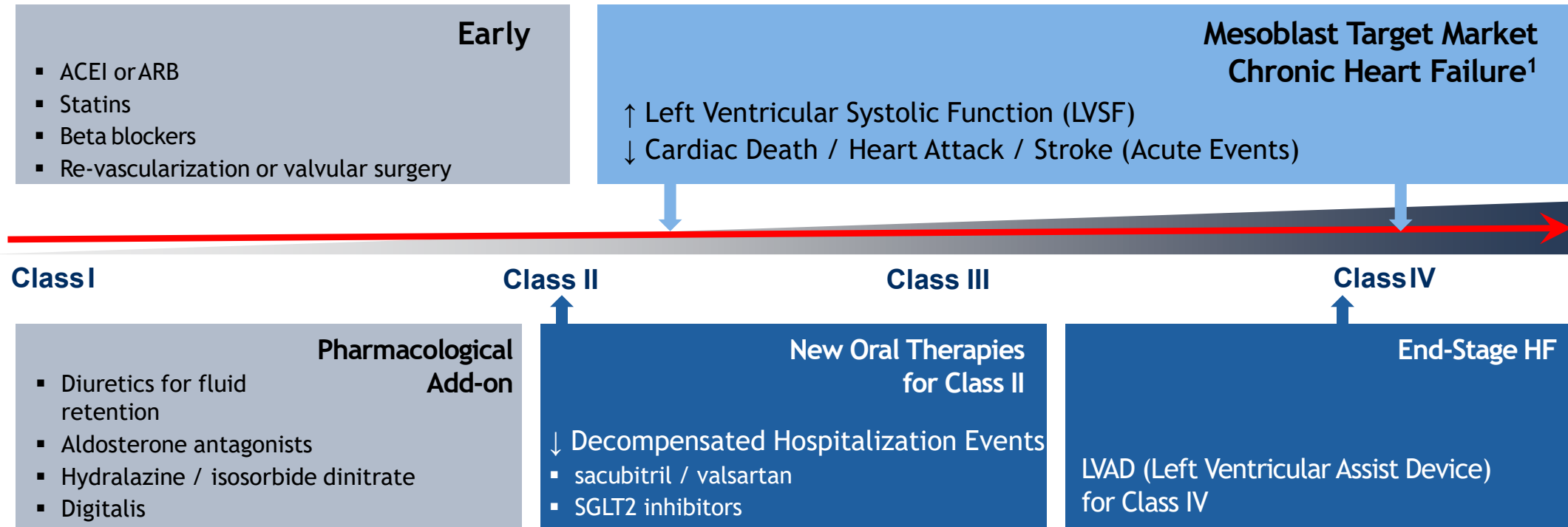
- ▣ Cardiovascular disease (CVD) remains the leading cause of death in the United States¹
- ▣ Heart failure affects 6.5 million patients in the US and 26 million patients globally. As populations age, the prevalence is increasing²
- ▣ Chronic heart failure is a progressive disease with a high mortality that approaches 50% at 5 years^{2,3} and at least 75% after an initial hospitalization⁴
- ▣ Patients with heart failure are also at high risk of recurrent major adverse cardiac events involving large vessels (heart attacks / strokes)

Patients Experience Progressive Vascular Dysfunction and Heart Failure

Rexlemestrocel-L has the potential to improve endothelial dysfunction in patients from Class II thru IV

Treatment Algorithm in Progressive Heart Failure (HF)

Progressive Vascular (Endothelial) Dysfunction and Heart Failure



Rexlemestrocel-L: DREAM Phase 3 Trial in Heart Failure (HFrEF)

Improvement in Left Ventricular Systolic Function, as Measured by Left Ventricular Ejection Fraction (LVEF) at 12 Months represents a potential early surrogate endpoint

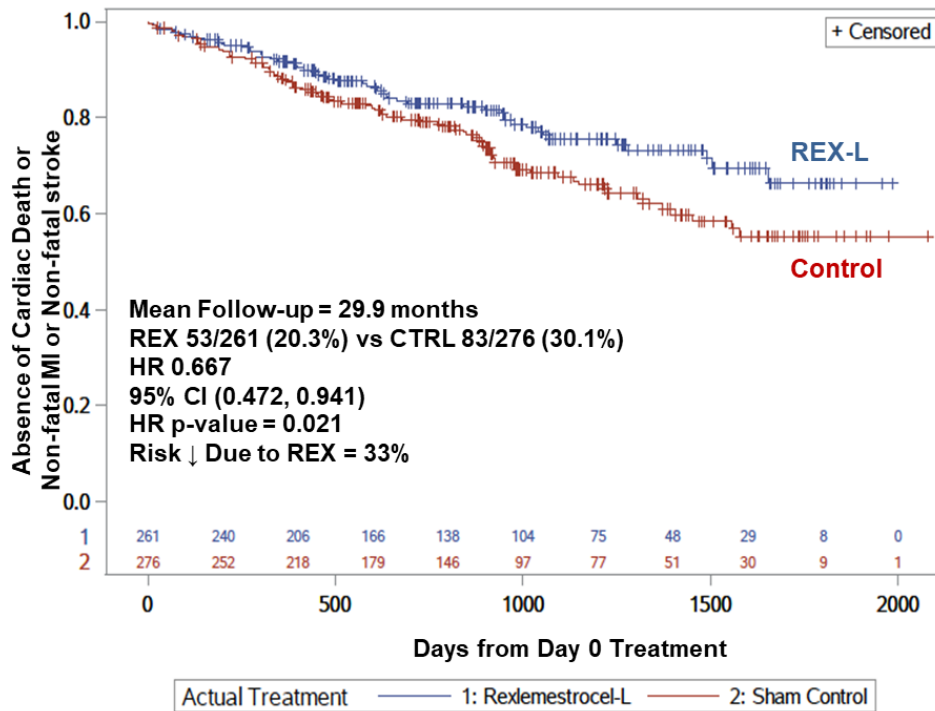
- ▣ In all treated patients (n=537), rexlemestrocel-L resulted in a 52% greater increase in LVEF from baseline to 12 months compared with controls
- ▣ While both groups had similar LVEF at baseline (28.7% and 28.6%), at 12 months, the least squared mean change from baseline was 5.0 for the rexlemestrocel-L group and 3.3 for controls (p=0.021)
- ▣ In treated patients with CRP >2 (n=301), rexlemestrocel-L resulted in 86% greater increase in LVEF from baseline to 12 months compared with controls
- ▣ While both groups had similar LVEF at baseline (29.1% and 28.2%), at 12 months, the least squared mean change from baseline was 5.6 for the rexlemestrocel-L group and 2.9 for controls (p=0.005)

DREAM-HF Phase 3 Trial in HFrEF

Rexlemestrocel-L reduced incidence of 3-Point Composite MACE v. controls across all treated patients, with enhanced effect in those with active inflammation as measured by CRP >2

All Treated Patients (n=537)

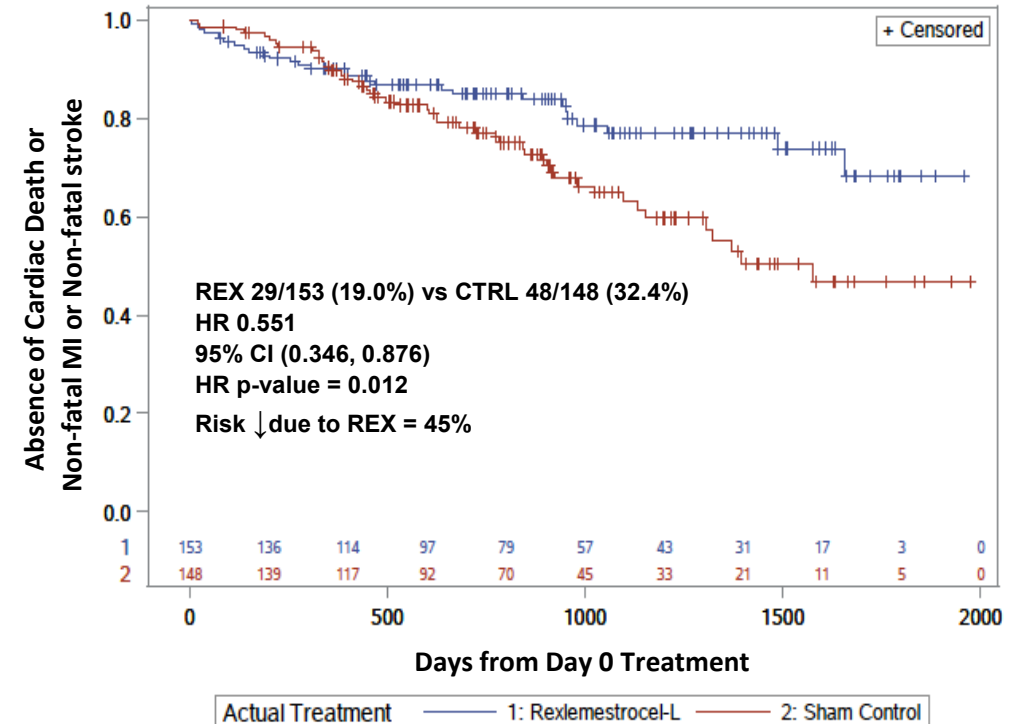
TTFE for 3-Point Composite MACE



Kaplan-Meier log rank statistics

All Treated Patients with hsCRP ≥2 (n=301)

TTFE for 3-Point Composite MACE



MACE=Major Adverse Cardiovascular Event; 3-Point Composite MACE=Cardiovascular Death, Non-Fatal MI or Non-Fatal Stroke; TTFE=Time To First Event; MI=Myocardial Infarction (Heart Attack); hsCRP=High Sensitivity C-reactive Protein (a measure of systemic inflammation)

Rexlemestrocel-L / HFrEF

Defining the Regulatory Path to FDA Approval



Significant Need

Cardiovascular disease remains the leading cause of death in the US

CHF is a progressive disease with a high mortality approaching 50% at 5 years, and at least 75% after an initial hospitalization



Promising Data

Recent data from the DREAM P3 trial showed improved LVEF at 12 months, preceding long-term reduction in MACE events across all treated patients

LVEF is a potential early surrogate endpoint



Targeting Inflammation

Effects on LVEF and MACE outcomes are enhanced in patients with active inflammation

Trial results from class II to end-stage HFrEF now support a MOA by which rexlemestrocel-L reverses inflammation-related endothelial dysfunction



H1 CY2023 FDA Meeting

Mesoblast plans to meet with the FDA in H1 CY2023 under its Regenerative Medicine Advanced Therapy (RMAT) designation to discuss the potential pathway to approval

The Makings of a Potential Banner Year for Mesoblast



January 2023

BLA resubmission for remestemcel-L/SR-aGVHD

H1 CY2023

Initiate pivotal Phase 3 study rexlemestrocel-L/CLBP

H2 CY2023

Estimated product launch for remestemcel-L/SR-aGVHD

H1 CY2023

FDA meeting for rexlemestrocel-L/HFrEF

Mid-CY2023

PDUFA date for remestemcel-L/SR-aGVHD



Thank You
